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009584646
WPI Acc No: 1993-278192/199335
XRAM Acc No: C93-124043

Vascular endothelial cell function improvers - contains fenofibrate e.g. isopropyl 2-(p-(p-chlorobenzoyl)phenoxy)-2-methyl propionate

Patent Assignee: GRELAN PHARM CO LTD (GREM)
Number of Countries: 001 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
JP 5194209	A	19930803	JP 9246423	A	19920121	199335	B

Priority Applications (No Type Date): JP 9246423 A 19920121
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
JP 5194209	A		5	A61K-031/22	

Abstract (Basic): JP 5194209 A

Vascular endothelial cells function improvers contain fenofibrate.

Fenofibrate, whose chemical nomenclature is isopropyl 2-(p-(p-chlorobenzoyl)phenoxy)-2-methylpropionate, is a worldwide employed drug treating hyperlipidemia. The agents can be administered orally or parentally alone or in combination with other pharmaceutically acceptable additives. Oral doses of this main effective component will be 10-800mg, 5-300mg, and 5-400mg by oral, injection, and mucous membrane route, resp.

USE/ADVANTAGE - Fenofibrate can improve or protect the deterioration of vascular endothelial functions. And therefore the present agents with its high safety in toxicity are potently useful in the prevention and treatment of arteriosclerosis, hypertension, and diabetes mellitus.

In an example, one tablet contained 100mg fenofibrate, 80mg crystallised cellulose, 48mg lactose, 20mg corn starch, and 2mg stearate. The tablet was prepd. conventionally according to the general rules for prepns. of tablets in the Japanese Phamacopoeia

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Title Terms: VASCULAR; ENDOTHELIUM; CELL; FUNCTION; IMPROVE; CONTAIN; ISOPROPYL; P; P; CHLORO; BENZOYL; PHENOXY; METHYL; PROPIONATE
Derwent Class: B05
International Patent Class (Main): A61K-031/22
International Patent Class (Additional): C07C-069/712
File Segment: CPI
Manual Codes (CPI/A-N): B10-F02; B12-F05; B12-H03; B12-H05
Chemical Fragment Codes (M2):
01 G013 G019 G100 H5 H541 H6 H602 H641 H8 J0 J011 J2 J271 J5 J581 M210 M213 M232 M272 M281 M313 M321 M331 M340 M342 M349 M381 M391 M414 M510 M520 M532 M540 M781 M903 M904 P526 P814 P816 R07499-U
Specific Compound Numbers: R07499-U

4/23/20

009637855
WPI Acc No: 1993-331404/199342
XRAM Acc No: C93-146786

Prepn. of 3-((R)-1-(substd. oxycarbonyloxy)ethyl)-4-substd.-2-azetidinone - by reacting hydroxyethyl-substd. azetidinone and haloformate, in presence of pyridine@, for use as intermediates for penem type antibacterial agents

Patent Assignee: TAKEDA CHEM IND LTD (TAKE)
Number of Countries: 001 Number of Patents: 001
Abstract (Basic): JP 5239020 A

Prepn. of 3-((R)-1-substd. oxycarbonyloxy)ethyl)-4-substd. -2-azetidinone comprises reacting 3-((R)-1-hydroxyethyl)-4, -substd. -2-azetidinone and haloformate in presence of pyridine and cpd. of formula (I). (R = lower alkyl; n - 1-3).

Organic solvents are pref. used in the prepn.. The organic solvents are ethers or esters. The n is 2 or 3. R is substd. on 2- or 6- carbon. The R is methyl. Cpd. (I) is 2.6-lutidine. Cpd. (I) is 2,4,6-collidine.

USE/ADVANTAGE - As intermediates for carbapenem and penem type antibacterial agents. The method gives 81-96%.

In an example, (3R,4R)-4-acetoxy-3-((R)-1 -hydroxyethyl)-2-azetinodine (5.19g) was dissolved in dry THF (120 mlO, and 2,6-lutidine (6.99 ml) and pyridine (0.48 ml) were added, the allyl chloroformate (3.18 ml) was added and stirred at 30 deg.C.. Every 1h allyl chloroformate (3.18 ml) was added three times, then the reaction mixt. was stirred at 30 deg.C. for 2hr.. To the residue given by evapn. ethyl acetate (200 ml) and 1N HCl (50 ml) were added and stirred. The organic layer was sepd. and washed with satd. copper sulphate then satd. aq. sodium chloride, and dried with magnesium sulphuric anhydride. The residue given by evapn. was purified by silica gel column chromatography (silica gel, 140g; ethyl acetate: hexane - 1:2) to give (3R,4R)-4-acetoxy-3-((R)-1-(allyl oxycarbonyloxy)ethyl) -2-azetidinone as pale yellow oil (6.95f, 90% yield). IR(Neat): 2980, 1790, 1750 cm-1; 1H-NMR(CDCl3) delta: 1.46 (3H, d, J=6.2Hz), 2.12 (3H,s), 3.37 (1H,dd, J=1-4, 6.8Hz), 4.6-4.7 (2H.m), 5.12 (1H,dq, J=6.8, 6.2Hz). 5.29 (1H,dq, J=10.4, 1.4Hz), 5.36 (1H,dq, J=17.4, 1.4Hz). 5.35 (1H,d, J=1.4Hz), 5.94 (1H,ddt, J=10.4, 17.4, 5.8Hz), 6.53 (1H, brs).

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Title Terms: PREPARATION; SUBSTITUTE; OXY; CARBONYLOXY; ETHYL; SUBSTITUTE; AZETIDINONE; REACT; HYDROXYETHYL; SUBSTITUTE; AZETIDINONE; HALOFORMATE; PRESENCE; PYRIDINE; INTERMEDIATE; PENEM; TYPE; ANTIBACTERIAL; AGENT
Derwent Class: B03
International Patent Class (Main): C07D-205/08
International Patent Class (Additional): B01J-031/02; C07B-061/00

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